

Blood pressure targets – a dynamic concept

Leonida Gherasim *

Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

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Establishing blood pressure targets for both diastolic (DBP) and systolic (SBP) values in managing hypertension (HTN) has become a central focus for many scientific and academic societies (with a professional profile in hypertension, cardiology, diabetes mellitus, nephrology). The need to define these targets has been obviated through various clinical studies, showing the benefit of steady BP values <140/90 mmHg on cardiovascular risk.

Guidelines on 'arithmetic' treatment targets have been elaborated not only in the management of hypertension (HTN), but also in the treatment of diabetes (HbA1C), dyslipidemia (particularly for LDL-C and TG), treatment with oral anticoagulants etc. For the majority of these conditions, targets to define therapeutic efficacy are constantly reevaluated through clinical studies analysis or reanalysis and the addition of novel therapeutic agents in treatment regimens.

In the past 10 years, the recommended BP target values in the prevention and management of hypertension have undergone significant modification. Hence, the 2007 ESH/ESC guidelines recommended

for patients at low-to-moderate risk a BP target value of <140/90 mmHg, and a target value of <130/80 mmHg for patients at high risk. The high-risk patients category included hypertensive patients with history of MI, stroke or kidney disease; for patients with diabetes mellitus (DM) and albuminuria, the recommended BP target value was of 120/75 mmHg [1].

Previous recommendations from the guidelines (elaborated by the JNC and the ESC/ESH) most implemented in clinical practice have been modified to a certain extent. For example, the JNC 8 (2014) recommended a BP target value of <140/90 mmHg overall [2], whereas the 2013 ESC/ESH guidelines classified BP target values according to risk. Therefore, in patients at low-to-moderate risk establishing a treatment BP target value of <140 mmHg received a class IB indication, whereas the same treatment goal in patients with DM was ascribed a class IA indication. Patients with coronary heart disease, history of stroke or TIAs and patients with diabetic or non-diabetic CKD had a class II A/B recommendation of BP target value of <140 mmHg [3].

The target value of <140/90 mmHg represents a general recommendation in the ESC/ESH guidelines for all stages of hypertension, with or without additional risk factors or target-organ damage. In selected cases, other target values can be established, for both SBP and DBP.

* Correspondence to: Prof. Leonida GHERASIM, MD, PhD
Carol Davila University of Medicine and Pharmacy,
Bucharest, Romania.

The elderly, particularly those over 80 years of age, have predominantly isolated systolic HTN, with DBP values <80 mmHg. Studies focusing on elderly patients with hypertension have showed benefits in cardiovascular events reduction for both SBP values <140 mmHg and <150 mmHg, respectively. However, in many cases such targets are not easily obtainable, and these patients are usually treated with triple therapy or maximal therapy (requiring diuretics), difficult to tolerate. The 2013 ESC/ESH guidelines maintain a class IA or IB recommendation for both target values, depending on individual tolerability and adjusting dosage, when needed.

In elderly patients with systolic HTN, the cerebrovascular risk is greater than the cardiac (coronary event) risk, therefore BP target values should be established after Doppler assessment of cervical and cranial arteries, particularly if clinical or imaging aspects of cerebrovascular disease are present, including cognitive impairment.

Special consideration should be given to optimal BP values in patients with DM, with or without albuminuria. Current ESC/ESH guidelines recommend a target value of <140/90 mmHg, however previous recommendations (European and American) have differed, with the European guideline recommending a target value of <140/85 mmHg, while the American guideline recommended a target value of <130/80 mmHg. Important data regarding hypertension treatment in patients with DM were extracted from the ACCORD-BP study [4]. The study researched the effects on cardiovascular events (MI, stroke, mortality) with 2 types of treatment regimens: intensive treatment with an established target value of <120 mmHg, compared to standard treatment and a target value of <140 mmHg. At a mean follow-up of 4.7 years, there was no significant difference on composite end-points between the 2 groups. Adverse events (due to BP values and complex therapy) have been more numerous in the intensive treatment group (3.3 % vs 1.3%, $p < 0.001$). Data from the ACCORD-BP study present an argument for a treatment 'target' in BP associated with DM of <140/90 mmHg. Nevertheless, the 2013 ESC/EASD guidelines on diabetes and cardiovascular disease management recommend a BP target value of <140/85 mmHg in patients with diabetes and HTN, however a lower target value (<130 mmHg) should be considered in patients with nephropathy, if tolerated [5].

A recent meta-analysis (2015) showed that a 10 mmHg reduction in SBP in patients with DM is associated with a 13% reduction in all-cause mortality, a 15% reduction in cardiovascular events and a 27% reduction in stroke, respectively [6]. The benefits of treatment particularly regard microvascular events and are due to a per se reduction in BP values [7].

Another special consideration concerning optimal BP values should also be given to patients with CKD – diabetic or non-diabetic. The 2013 ESC/ESH guidelines recommend maintaining the BP values <140/90 mmHg, however the KDOQI recommends a target value of <140/80 mmHg if no albuminuria present, or <130/80 mmHg with associated albuminuria [8]. While researching the benefits of various BP target values in patients with CKD, as well as in diabetic patients, it is important to establish the impact of lower BP values on kidney function.

In summary, the currently recommended BP target values in the treatment of various types of hypertension associate a degree of uncertainty and relativity. In clinical practice, there are many options possible concerning BP target values. Recently, the SPRINT study has reignited the discussion on optimal treatment targets in hypertension.

The SPRINT study was sponsored by the NHLBI (National Heart, Lung and Blood Institute) and other National Institutes in the US. The study enrolled 9361 patients with SBP >130 mmHg and at high cardiovascular risk, treated and followed-up for a mean of 3.6 years. Patients were assigned to either a standard treatment group (BP target value <140 mmHg) or an intensive treatment group (BP target value <120 mmHg). The composite end-point consisted of acute coronary syndromes (including MI), stroke, acutely decompensated heart failure and cardiovascular-related death [9].

The intensive treatment group had a significant reduction in the composite end-point compared to the standard treatment group (1.65% vs 2.14%). After 3.6 years of follow-up, the mean SBP was 121.5 mmHg in the intensive treatment group, and 134.6 mmHg in the standard treatment group, respectively. However, numerous severe adverse events (hypotension, syncope, electrolyte disorders, acute kidney injury) were reported in the former group (4.7% vs 2.1%).

The results gathered from SPRINT demonstrate that, at least in patients with hypertension grade I and II and non-diabetic, reduction of BP values <120 mmHg

with intensive treatment is associated with a reduction in cardiovascular risk. However, these results cannot be extrapolated to patients with severe hypertension, diabetes, CKD (renal dysfunction) or history of stroke. Consequently, the SPRINT study is challenging the multiple specialties dealing with hypertensive patients and experts participating in elaborating guidelines.

Will current BP target values change over the next period, based solely on the results of a clinical study, regardless of its rigorous conduction? In the ACCORD-BP study, with similar design and objectives as SPRINT (BP values <120 mmHg), the results concerning diabetic patients did not reach statistical significance for reduction in the primary end-point, except for stroke. Combining the data from SPRINT and ACCORD-BP, one can conclude there is a reduction in the primary end-point and individual components with intensive treatment.

The diversity of data concerning BP target values in the treatment of hypertension, the guidelines elaborated by professional societies, as well as recent clinical studies point to the conclusion that the recommended target values carry relative uncertainty, explainable through the wide diversity of the hypertension syndrome.

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